

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

## PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/IB2004/001723

International filing date (day/month/year)  
19.05.2004

Priority date (day/month/year)  
23.05.2003

International Patent Classification (IPC) or both national classification and IPC  
C07D413/04, C07D413/14, C07D417/14, A61K31/4245

Applicant  
APONETICS AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

10/557539

International application No.  
PCT/IB2004/001723

IP20 Rec'd PCT/PTO 21 NOV 2005

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/IB2004/001723

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**Box No. II    Priority**

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1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/IB2004/001723

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 21 (partly)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 21 (partly)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/IB2004/001723

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	1-22
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-22
Industrial applicability (IA)	Yes: Claims	1-22
	No: Claims	

2. Citations and explanations

**see separate sheet**

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**Box No. VI Certain documents cited**

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1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

**see form 210**

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**Box No. VIII Certain observations on the international application**

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The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

PCT/IB2004/001723

**Re Item III****Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claim 21 was only searched in as far as the compounds of the formula 1 according to claim 1 are concerned and their esters, (see description, page 10, lines 23-24), although it is noted that most of the definitions anyway comprise esters of any esterifiable groups.

**Re Item V****Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

The following documents cited in the search report are referred to in this communication;

- D1: SERGIEVSKII A V ET AL: "4-AMINOFURAZAN-3-CARBOXYLIC ACID IMINOESTER IN REACTIONS WITH N,O-NUCLEOPHILES" RUSSIAN JOURNAL OF ORGANIC CHEMISTRY, CONSULTANTS BUREAU, US, vol. 38, no. 6, 2002, pages 872-874, XP009018073 ISSN: 1070-4280
- D2: SERGIEVSKII A V ET AL: "REACTIONS OF METHYL 4-AMINOFURAZAN-3-CARBOXIMIDATE WITH NITROGEN-CONTAINING NUCLEOPHILES" RUSSIAN JOURNAL OF ORGANIC CHEMISTRY, CONSULTANTS BUREAU, US, vol. 37, no. 5, 2001, pages 717-720, XP001155338 ISSN: 1070-4280
- D3: DE 31 00 771 A (USV PHARMA CORP) 26 August 1982 (1982-08-26)

With regard to the requirement for novelty, the compounds of the present application claims 1-18 are novel with respect to D1-D3 on account of the 1,2,5 oxadiazole or the CH<sub>2</sub>-X-R grouping. The process claims and use claims are thus also novel. Article 33(2) of the PCT is thus satisfied.

~~With regard to the requirement for inventive step~~ (Article 33(3) of the PCT), the problem underlying the present application is seen as the provision of novel compounds with

use in the treatment of neoplastic and autoimmune diseases and processes for their preparation. The man skilled in the art, faced with this problem, would have had no incentive from the available prior art to prepare such compounds, expecting them to have this activity (D3 differs structurally and in activity, D1 and D2 disclose no activity). Thus for those compounds actually prepared and shown to solve the problem, and a reasonable generalisation thereof, an inventive step could be acknowledged. However, it is not considered to be plausible that all possible compounds falling under the general formula are obvious equivalents of those actually shown to be inventive, as the terms such as "heteroaryl", "optionally substituted" etc introduce possible structures into the claim which could contain other groups for which the activity could either not be predicted, or which indeed contain structures known to exhibit other qualitative activities. It would appear from the data given in the description, that certain examples do not actually show the desired activity. The Applicant is asked to provide technical substantiation for the extrapolation over the examples used before Article 33(3) of the PCT can be considered to be satisfied. For the process of preparation, this could be considered to be analogous to D1 and D2 preparations, and thus unless all of the compounds are shown to be inventive, this process is considered obvious in the light of D1 and D2.

**Re Item VI**

**Certain documents cited**

**Certain published documents**

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO-03066629	14.08.03	06.02.03	06.02.02

**Re Item VIII**

The Table 9 referred to in description, page 71 is not present